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 assignment/reassignment information  
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 NEWS 9 APR 28 Limits doubled for structure searching in CAS  
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 NEWS 12 MAY 11 BEILSTEIN substance information now available on  
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 NEWS 13 MAY 14 DGENE, PCTGEN and USGENE enhanced with increased  
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 NEWS 15 MAY 28 CAS databases on STN enhanced with NANO super role in  
 records back to 1992  
 NEWS 16 JUN 01 CAS REGISTRY Source of Registration (SR) searching  
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NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,  
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FILE 'HOME' ENTERED AT 10:09:16 ON 10 JUN 2009

=> file medline biosis caplus embase  
COST IN U.S. DOLLARS  
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ENTRY  
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TOTAL  
SESSION  
0.22

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 10:09:42 ON 10 JUN 2009

FILE 'BIOSIS' ENTERED AT 10:09:42 ON 10 JUN 2009  
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=> s KURIHARA H?/AU  
L1 3876 KURIHARA H?/AU

=> s l1 and periodon?  
L2 290 L1 AND PERIODON?

=> s l2 and neurotroph?  
L3 16 L2 AND NEUROTROPH?

=> dup rem 13  
PROCESSING COMPLETED FOR L3  
L4 5 DUP REM L3 (11 DUPLICATES REMOVED)

=> s Kawaguchi H?/au  
L5 5694 KAWAGUCHI H?/AU

=> s l5 and periodon?  
L6 78 L5 AND PERIODON?

=> s l6 and neurotroph?  
L7 12 L6 AND NEUROTROPH?

=> dup rem 17  
PROCESSING COMPLETED FOR L7  
L8 4 DUP REM L7 (8 DUPLICATES REMOVED)

=> s takeda K?/au  
L9 14861 TAKEDA K?/AU

=> s l9 and periodon?  
L10 41 L9 AND PERIODON?

=> s l10 and neurotroph?  
L11 16 L10 AND NEUROTROPH?

=> dup rem 111  
PROCESSING COMPLETED FOR L11  
L12 5 DUP REM L11 (11 DUPLICATES REMOVED)

=> s shiba h?/au  
L13 818 SHIBA H?/AU

=> s l13 and periodon?

L14 118 L13 AND PERIODON?

=> s l14 and neurotroph?  
L15 16 L14 AND NEUROTROPH?

=> dup rem 115  
PROCESSING COMPLETED FOR L15  
L16 5 DUP REM L15 (11 DUPLICATES REMOVED)

=> mizuno n?/au  
MIZUNO IS NOT A RECOGNIZED COMMAND  
The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> s mizuno n?/au  
L17 3797 MIZUNO N?/AU

=> s l17 and periodon?  
L18 52 L17 AND PERIODON?

=> s l18 and neurotroph?  
L19 12 L18 AND NEUROTROPH?

=> dup rem 119  
PROCESSING COMPLETED FOR L19  
L20 4 DUP REM L19 (8 DUPLICATES REMOVED)

=> s yoshino h?/au  
L21 3348 YOSHINO H?/AU

=> s l21 and periodon?  
L22 30 L21 AND PERIODON?

=> s l22 and neurotroph?  
L23 9 L22 AND NEUROTROPH?

=> dup rem 123  
PROCESSING COMPLETED FOR L23  
L24 3 DUP REM L23 (6 DUPLICATES REMOVED)

=> s hasegawa n?/au  
L25 2635 HASEGAWA N?/AU

=> s l25 and periodon?  
L26 27 L25 AND PERIODON?

=> s l26 and neurotroph?  
L27 8 L26 AND NEUROTROPH?

=> dup rem 127  
PROCESSING COMPLETED FOR L27  
L28 3 DUP REM L27 (5 DUPLICATES REMOVED)

=> shinohara h?/au  
SHINOHARA IS NOT A RECOGNIZED COMMAND  
The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> s shinohara h?/au  
L29 3603 SHINOHARA H?/AU

```
=> s 129 and periodon?
L30          24 L29 AND PERIODON?

=> s 130 and neurotroph?
L31          5 L30 AND NEUROTROPH?

=> dup rem 131
PROCESSING COMPLETED FOR L31
L32          2 DUP REM L31 (3 DUPLICATES REMOVED)

=> dis his

(FILE 'HOME' ENTERED AT 10:09:16 ON 10 JUN 2009)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 10:09:42 ON 10 JUN 2009
L1          3876 S KURIHARA H?/AU
L2          290 S L1 AND PERIODON?
L3          16 S L2 AND NEUROTROPH?
L4          5 DUP REM L3 (11 DUPLICATES REMOVED)
L5          5694 S KAWAGUCHI H?/AU
L6          78 S L5 AND PERIODON?
L7          12 S L6 AND NEUROTROPH?
L8          4 DUP REM L7 (8 DUPLICATES REMOVED)
L9          14861 S TAKEDA K?/AU
L10         41 S L9 AND PERIODON?
L11         16 S L10 AND NEUROTROPH?
L12         5 DUP REM L11 (11 DUPLICATES REMOVED)
L13         818 S SHIBA H?/AU
L14         118 S L13 AND PERIODON?
L15         16 S L14 AND NEUROTROPH?
L16         5 DUP REM L15 (11 DUPLICATES REMOVED)
L17         3797 S MIZUNO N?/AU
L18         52 S L17 AND PERIODON?
L19         12 S L18 AND NEUROTROPH?
L20         4 DUP REM L19 (8 DUPLICATES REMOVED)
L21         3348 S YOSHINO H?/AU
L22         30 S L21 AND PERIODON?
L23         9 S L22 AND NEUROTROPH?
L24         3 DUP REM L23 (6 DUPLICATES REMOVED)
L25         2635 S HASEGAWA N?/AU
L26         27 S L25 AND PERIODON?
L27         8 S L26 AND NEUROTROPH?
L28         3 DUP REM L27 (5 DUPLICATES REMOVED)
L29         3603 S SHINOHARA H?/AU
L30         24 S L29 AND PERIODON?
L31         5 S L30 AND NEUROTROPH?
L32         2 DUP REM L31 (3 DUPLICATES REMOVED)
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=> dis ibib abs 14 1-5

L4 ANSWER 1 OF 5      MEDLINE on STN          DUPLICATE 1
ACCESSION NUMBER: 2008408883      MEDLINE
DOCUMENT NUMBER: PubMed ID: 18390540
TITLE: Brain-derived neurotrophic factor stimulates
       bone/cementum-related protein gene expression in
       cementoblasts.
AUTHOR: Kajiya Mikihito; Shiba Hideki; Fujita Tsuyoshi; Ouhara
       Kazuhisa; Takeda Katsuhiro; Mizuno Noriyoshi; Kawaguchi
       Hiroyuki; Kitagawa Masaë; Takata Takashi; Tsuji Koichiro;
       Kurihara Hidemi
CORPORATE SOURCE: Department of Periodontal Medicine, Hiroshima University
```

SOURCE: Graduate School of Biomedical Sciences, Minami-ku,  
Hiroshima 34-8553, Japan.  
The Journal of biological chemistry, (2008 Jun 6) Vol. 283,  
No. 23, pp. 16259-67. Electronic Publication: 2008-04-03.  
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200807  
ENTRY DATE: Entered STN: 27 Jun 2008  
Last Updated on STN: 16 Jul 2008  
Entered Medline: 15 Jul 2008

AB Brain-derived neurotrophic factor (BDNF), recognized as essential in the developing nervous system, is involved in differentiation and proliferation in non-neuronal cells, such as endothelial cells, osteoblasts, and periodontal ligament cells. We have focused on the application of BDNF to the regeneration of periodontal tissue and indicated that BDNF promotes the regeneration of experimentally created periodontal defects. Cementoblasts form cementum, mineralized tissue, which is key to establishing a functional periodontium. The application of BDNF to the regeneration of periodontal tissue requires elucidation of the mechanism by which BDNF regulates the functions of cementoblasts. In this study, we examined how BDNF regulates the mRNA expression of bone/cementum-related proteins (alkaline phosphatase (ALP), osteopontin (OPN), and bone morphogenetic protein-2 (BMP-2)) in cultures of immortalized human cementoblast-like (HCEM) cells. BDNF elevated the mRNA levels of ALP, OPN, and BMP-2 in HCEM cells. Small interfering RNA (siRNA) for TRKB, a high affinity receptor of BDNF, siRNA for Elk-1, which is a downstream target of ERK1/2, and PD98059, an ERK inhibitor, obviated the increase in the mRNA levels. BDNF increased the levels of phosphorylated ERK1/2 and Elk-1, and the blocking of BDNF signaling by treatment with siRNA for TRKB and PD98059 suppressed the phosphorylation of ERK1/2 and Elk-1. Furthermore, BDNF increased the levels of phosphorylated c-Raf, which activates the ERK signaling pathway. These findings provide the first evidence that the TrkB-c-Raf-ERK1/2-Elk-1 signaling pathway is required for the BDNF-induced mRNA expression of ALP, OPN, and BMP-2 in HCEM cells.

L4 ANSWER 2 OF 5 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2008714203 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18980528  
TITLE: Effect of neurotrophin-4/5 on bone/cementum-related protein expressions and DNA synthesis in cultures of human periodontal ligament cells.  
AUTHOR: Mizuno Noriyoshi; Shiba Hideki; Inui Takafumi; Takeda Katsuhiro; Kajiyama Mikihito; Hasegawa Nachiko; Kawaguchi Hiroyuki; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.. mizuno@hiroshima-u.ac.jp  
SOURCE: Journal of periodontology, (2008 Nov) Vol. 79, No. 11, pp. 2182-9.  
Journal code: 8000345. ISSN: 0022-3492.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Dental Journals; Priority Journals  
ENTRY MONTH: 200902  
ENTRY DATE: Entered STN: 5 Nov 2008

Last Updated on STN: 15 Feb 2009  
Entered Medline: 12 Feb 2009

AB BACKGROUND: We studied neurotrophins (NTs) as signaling molecules for periodontal tissue regeneration and showed that nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) modulate the proliferation and differentiation of human periodontal ligament (HPL) cells in vitro. The purpose of this study was to investigate whether NT-4/5 also has the ability to regulate the function of HPL cells. METHODS: mRNA expressions of NT-4/5 and its high-affinity tyrosine kinase receptor (trkB) were analyzed in HPL cells by reverse transcription-polymerase chain reaction. We examined how NT-4/5 regulates the mRNA expression of bone/cementum-related proteins (alkaline phosphatase [ALPase], osteopontin [OPN], osteocalcin [OC], and bone morphogenetic protein [BMP]-2) in cultures of HPL cells. Moreover, the effects of NT-4/5 on calcification, the production of OPN and OC, and DNA synthesis in HPL cells were examined. RESULTS: NT-4/5 and trkB mRNA were expressed in HPL cells. NT-4/5 elevated the mRNA levels of ALPase, OPN, OC, and BMP-2 and the syntheses of OPN, OC, and DNA in HPL cells. PD98059, an extracellular signal-regulated kinase (ERK) inhibitor, obviated the increase in the mRNA levels of ALPase, OPN, OC, and BMP-2. NT-4/5 increased the levels of phosphorylated ERK1/2. Furthermore, NT-4/5 enhanced the amount of mineral deposits in cultures of HPL cells. CONCLUSION: NT-4/5, as well as BDNF and NGF, is suggested to play a role in the regulation of function of periodontal ligament cells.

L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2005:259902 CAPLUS  
DOCUMENT NUMBER: 142:303690  
TITLE: Remedy and therapeutic method for periodontal diseases and pulpal diseases with neurotrophic factors  
INVENTOR(S): Kurihara, Hidemi; Kawaguchi, Hiroyuki; Takeda, Katsuhiro; Shiba, Hideki; Mizuno, Noriyoshi; Yoshihino, Hiroshi; Hasegawa, Neohiko; Shinohara, Hiroaki  
PATENT ASSIGNEE(S): Two Cells Co. Ltd., Japan  
SOURCE: PCT Int. Appl., 86 pp.  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025605	A1	20050324	WO 2004-JP13023	20040908
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JE, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004271843	A1	20050324	AU 2004-271843	20040908
EP 1671641	A1	20060621	EP 2004-787706	20040908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1871024	A	20061129	CN 2004-80031194	20040908

RU 2336089	C2	20081020	RU 2006-111465	20040908
US 20070071693	A1	20070329	US 2006-571069	20061207
PRIORITY APPLN. INFO.:			JP 2003-316719	A 20030909
			WO 2004-JP13023	W 20040908

AB It is intended to provide a remedy and a therapeutic method for periodontal diseases and pulpal diseases, a transplantation material for regenerating a periodontal tissue and a method of regenerating a periodontal tissue. Namely, a remedy for periodontal diseases and pulpal diseases comprising a neurotrophic factor as the active ingredient. The effect of brain-derived neurotrophic factor (BDNF) on cultured human periodontal ligament cell and human gingival keratinocyte was examined.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 5 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 2005583578 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 16259615  
TITLE: Brain-derived neurotrophic factor enhances periodontal tissue regeneration.  
AUTHOR: Takeda Katsuhiro; Shiba Hideki; Mizuno Noriyoshi; Hasegawa Naohiko; Mouri Yoshihiro; Hirachi Akio; Yoshino Hiroshi; Kawaguchi Hiroyuki; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.  
SOURCE: Tissue engineering, (2005 Sep-Oct) Vol. 11, No. 9-10, pp. 1618-29.  
Journal code: 9505538. ISSN: 1076-3279.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (COMPARATIVE STUDY)  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200512  
ENTRY DATE: Entered STN: 3 Nov 2005  
Last Updated on STN: 23 Dec 2005  
Entered Medline: 22 Dec 2005

AB To address whether brain-derived neurotrophic factor (BDNF) could be involved in periodontal tissue regeneration, we examined the effects of BDNF on proliferation and the expression of bone (cementum)- related proteins (osteopontin, bone morphogenetic protein [BMP]-2, type I collagen, alkaline phosphatase [ALPase], and osteocalcin) in cultures of human periodontal ligament (HPL) cells, which are thought to be prerequisite for periodontal tissue regeneration, and on proliferation and angiogenesis in human endothelial cells. Furthermore, we examined the effect of BDNF on the regeneration of periodontal tissues in experimentally induced periodontal defects in dogs. BDNF elevated the expression of ALPase and osteocalcin mRNAs and increased the synthesis of osteopontin, BMP-2, and type I collagen DNA in HPL cells. BDNF stimulated mRNA expression of vascular endothelial growth factor-B and tenascin-X, and proliferation and angiogenesis in human endothelial cells. In vivo studies showed that BDNF stimulated the formation of new alveolar bone cementum and connective new fibers, which were inserted into the newly formed cementum and bone. BDNF also stimulated blood capillary formation. These findings suggest that the regulation of functioning of periodontal ligament cells and endothelial cells by BDNF results in the promotion of periodontal tissue regeneration.

L4 ANSWER 5 OF 5 MEDLINE on STN DUPLICATE 4  
ACCESSION NUMBER: 2003081727 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12593600  
TITLE: Neurotrophins in cultured cells from periodontal tissues.  
AUTHOR: Kurihara Hidemi; Shinohara Hiroaki; Yoshino Hiroshi; Takeda Katsuhiro; Shiba Hideki  
CORPORATE SOURCE: Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of Biomedical Science, Hiroshima, Japan..  
hkuri@hiroshima-u.ac.jp  
SOURCE: Journal of periodontology, (2003 Jan) Vol. 74, No. 1, pp. 76-84. Ref: 67  
Journal code: 8000345. ISSN: 0022-3492.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Dental Journals; Priority Journals  
ENTRY MONTH: 200305  
ENTRY DATE: Entered STN: 21 Feb 2003  
Last Updated on STN: 8 May 2003  
Entered Medline: 7 May 2003

AB We review the basic functions of neurotrophins and their receptors and discuss the expression and functions of neurotrophins and their specific receptors based on recent data using cultured cells from human periodontal tissues. Neurotrophins, nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and neurotrophin-3 (NT-3) play crucial roles in the differentiation and survival of neural cells. Neurotrophins activate 2 different receptor classes: the tropomyosin-related kinase (Trk) family of receptor tyrosine kinases (TrkA, TrkB, and TrkC) and the p75 receptor, a member of the tumor necrosis factor receptor superfamily. Neurotrophins regulate both cell death and cell survival through activations of Trk receptors and/or p75 neurotrophin receptor. It has been reported that neurotrophins are also produced from non-neuronal cells, such as leukocytes, osteoblasts, or fibroblasts, and act in many other ways on non-neuronal cells. Neurotrophin expression during bone fracture healing is especially interesting, and neurotrophins are now implicated in hard tissue regeneration. It is well known that neurotrophins and their receptors are expressed in tooth development. Recent studies have found that neurotrophins and Trk receptors are expressed in mouse osteoblastic cell lines. Human periodontal ligament cells, human gingival fibroblasts, and human gingival keratinocytes expressed mRNA for NGF and TrkA. The secretion of bioactive NGF peptides from human periodontal ligament cells and human gingival keratinocytes was confirmed by bioassay using PC12 cells (rat adrenal pheochromocytoma cells). The expression of NGF and TrkA mRNA was regulated by interleukin (IL)-1 $\beta$ . NGF increased DNA synthesis and expressions of mRNA for bone-related proteins, alkaline phosphatase, and osteopontin in human periodontal ligament cells. Neurotrophins and Trk receptors expressed in human periodontal tissue may contribute to regeneration as well as innervation of periodontal tissue through local autocrine and paracrine pathways. Recent data suggest that some functions of neurotrophins and Trk receptors relate to periodontal disease and periodontal tissue regeneration. However, in vivo studies will be required to clarify the roles of neurotrophins and their receptors, including p75, in periodontal disease and periodontal tissue regeneration.

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COST IN U.S. DOLLARS  
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SESSION  
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CA SUBSCRIBER PRICE

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FILE CONTAINS CURRENT INFORMATION.  
LAST RELOADED: Jun 5, 2009 (20090605/UP).

=> dis ibib abs 18 1-4  
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, CAPLUS' - CONTINUE? (Y)/N:y

L8 ANSWER 1 OF 4 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2008408883 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18390540  
TITLE: Brain-derived neurotrophic factor stimulates  
bone/cementum-related protein gene expression in  
cementoblasts.  
AUTHOR: Kajiyama Mikihito; Shiba Hideki; Fujita Tsuyoshi; Ohara  
Kazuhisa; Takeda Katsuhiro; Mizuno Noriyoshi;  
Kawaguchi Hiroyuki; Kitagawa Masaë; Takata Takashi;  
Tsuiji Koichiro; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Hiroshima University  
Graduate School of Biomedical Sciences, Minami-ku,  
Hiroshima 34-8553, Japan.  
SOURCE: The Journal of biological chemistry, (2008 Jun 6) Vol. 283,  
No. 23, pp. 16259-67. Electronic Publication: 2008-04-03.  
Journal code: 2985121R. ISSN: 0021-9258.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200807  
ENTRY DATE: Entered STN: 27 Jun 2008  
Last Updated on STN: 16 Jul 2008  
Entered Medline: 15 Jul 2008  
AB Brain-derived neurotrophic factor (BDNF), recognized as  
essential in the developing nervous system, is involved in differentiation  
and proliferation in non-neuronal cells, such as endothelial cells,  
osteoblasts, and periodontal ligament cells. We have focused on  
the application of BDNF to the regeneration of periodontal  
tissue and indicated that BDNF promotes the regeneration of experimentally  
created periodontal defects. Cementoblasts form cementum,  
mineralized tissue, which is key to establishing a functional  
periodontium. The application of BDNF to the regeneration of  
periodontal tissue requires elucidation of the mechanism by which  
BDNF regulates the functions of cementoblasts. In this study, we examined  
how BDNF regulates the mRNA expression of bone/cementum-related proteins  
(alkaline phosphatase (ALP), osteopontin (OPN), and bone morphogenetic

protein-2 (BMP-2)) in cultures of immortalized human cementoblast-like (HCEM) cells. BDNF elevated the mRNA levels of ALP, OPN, and BMP-2 in HCEM cells. Small interfering RNA (siRNA) for TRKB, a high affinity receptor of BDNF, siRNA for Elk-1, which is a downstream target of ERK1/2, and PD98059, an ERK inhibitor, obviated the increase in the mRNA levels. BDNF increased the levels of phosphorylated ERK1/2 and Elk-1, and the blocking of BDNF signaling by treatment with siRNA for TRKB and PD98059 suppressed the phosphorylation of ERK1/2 and Elk-1. Furthermore, BDNF increased the levels of phosphorylated c-Raf, which activates the ERK signaling pathway. These findings provide the first evidence that the TrkB-c-Raf-ERK1/2-Elk-1 signaling pathway is required for the BDNF-induced mRNA expression of ALP, OPN, and BMP-2 in HCEM cells.

L8 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2008714203 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18980528  
TITLE: Effect of neurotrophin-4/5 on bone/cementum-related protein expressions and DNA synthesis in cultures of human periodontal ligament cells.  
AUTHOR: Mizuno Noriyoshi; Shiba Hideki; Inui Takafumi; Takeda Katsuhiro; Kajiyama Mikihito; Hasegawa Naohiko; Kawaguchi Hiroyuki; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.. mizuno@hiroshima-u.ac.jp  
SOURCE: Journal of periodontology, (2008 Nov) Vol. 79, No. 11, pp. 2182-9.  
JOURNAL CODE: 8000345. ISSN: 0022-3492.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Dental Journals; Priority Journals  
ENTRY MONTH: 200902  
ENTRY DATE: Entered STN: 5 Nov 2008  
Last Updated on STN: 15 Feb 2009  
Entered Medline: 12 Feb 2009

AB BACKGROUND: We studied neurotrophins (NTs) as signaling molecules for periodontal tissue regeneration and showed that nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) modulate the proliferation and differentiation of human periodontal ligament (HPL) cells in vitro. The purpose of this study was to investigate whether NT-4/5 also has the ability to regulate the function of HPL cells. METHODS: mRNA expressions of NT-4/5 and its high-affinity tyrosine kinase receptor (trkB) were analyzed in HPL cells by reverse transcription-polymerase chain reaction. We examined how NT-4/5 regulates the mRNA expression of bone/cementum-related proteins (alkaline phosphatase [ALPase], osteopontin [OPN], osteocalcin [OC], and bone morphogenetic protein [BMP]-2) in cultures of HPL cells. Moreover, the effects of NT-4/5 on calcification, the production of OPN and OC, and DNA synthesis in HPL cells were examined. RESULTS: NT-4/5 and trkB mRNA were expressed in HPL cells. NT-4/5 elevated the mRNA levels of ALPase, OPN, OC, and BMP-2 and the syntheses of OPN, OC, and DNA in HPL cells. PD98059, an extracellular signal-regulated kinase (ERK) inhibitor, obviated the increase in the mRNA levels of ALPase, OPN, OC, and BMP-2. NT-4/5 increased the levels of phosphorylated ERK1/2. Furthermore, NT-4/5 enhanced the amount of mineral deposits in cultures of HPL cells. CONCLUSION: NT-4/5, as well as BDNF and NGF, is suggested to play a role in the regulation of function of periodontal ligament cells.

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2005:259902 CAPLUS

DOCUMENT NUMBER: 142:303690  
 TITLE: Remedy and therapeutic method for periodontal diseases and pulpal diseases with neurotrophic factors  
 INVENTOR(S): Kurihara, Hidemi; Kawaguchi, Hiroyuki; Takeda, Katsuhiro; Shiba, Hideki; Mizuno, Noriyoshi; Yoshino, Hiroshi; Hasegawa, Naohiko; Shinohara, Hiroaki  
 PATENT ASSIGNEE(S): Two Cells Co. Ltd., Japan  
 SOURCE: PCT Int. Appl., 86 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025605	A1	20050324	WO 2004-JP13023	20040908
W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	A1	20050324	AU 2004-271843	20040908
EP 1671641	A1	20060621	EP 2004-787706	20040908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK	A	20061129	CN 2004-80031194	20040908
CN 1871024	A	20061129	CN 2004-80031194	20040908
RU 2336089	C2	20081020	RU 2006-111465	20040908
US 2007071693	A1	20070329	US 2006-571069	20061207
PRIORITY APPLN. INFO.:			JP 2003-316719	A 20030909
			WO 2004-JP13023	W 20040908

**AB** It is intended to provide a remedy and a therapeutic method for periodontal diseases and pulpal diseases, a transplantation material for regenerating a periodontal tissue and a method of regenerating a periodontal tissue. Namely, a remedy for periodontal diseases and pulpal diseases comprising a neurotrophic factor as the active ingredient. The effect of brain-derived neurotrophic factor (BDNF) on cultured human periodontal ligament cell and human gingival keratinocyte was examined

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 4	MEDLINE on STN	DUPPLICATE 3
ACCESSION NUMBER: 2005583578	MEDLINE	
DOCUMENT NUMBER: 16259615		
TITLE: Brain-derived neurotrophic factor enhances periodontal tissue regeneration.		
AUTHOR: Takeda Katsuhiro; Shiba Hideki; Mizuno Noriyoshi; Hasegawa Naohiko; Mouri Yoshihiro; Hirachi Akio; Yoshino Hiroshi; Kawaguchi Hiroyuki; Kurihara Hidemi		
CORPORATE SOURCE: Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.		

SOURCE: Tissue engineering, (2005 Sep-Oct) Vol. 11, No. 9-10, pp. 1618-29.  
Journal code: 9505538. ISSN: 1076-3279.

PUB. COUNTRY: United States  
DOCUMENT TYPE: (COMPARATIVE STUDY)  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200512  
ENTRY DATE: Entered STN: 3 Nov 2005  
Last Updated on STN: 23 Dec 2005  
Entered Medline: 22 Dec 2005

AB To address whether brain-derived neurotrophic factor (BDNF) could be involved in periodontal tissue regeneration, we examined the effects of BDNF on proliferation and the expression of bone (cementum)- related proteins (osteopontin, bone morphogenetic protein [BMP]-2, type I collagen, alkaline phosphatase [ALPase], and osteocalcin) in cultures of human periodontal ligament (HPL) cells, which are thought to be prerequisite for periodontal tissue regeneration, and on proliferation and angiogenesis in human endothelial cells. Furthermore, we examined the effect of BDNF on the regeneration of periodontal tissues in experimentally induced periodontal defects in dogs. BDNF elevated the expression of ALPase and osteocalcin mRNAs and increased the synthesis of osteopontin, BMP-2, and type I collagen DNA in HPL cells. BDNF stimulated mRNA expression of vascular endothelial growth factor-B and tenascin-X, and proliferation and angiogenesis in human endothelial cells. In vivo studies showed that BDNF stimulated the formation of new alveolar bone cementum and connective new fibers, which were inserted into the newly formed cementum and bone. BDNF also stimulated blood capillary formation. These findings suggest that the regulation of functioning of periodontal ligament cells and endothelial cells by BDNF results in the promotion of periodontal tissue regeneration.

=> dis ibib abs l12 1-5  
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, CAPLUS' - CONTINUE? (Y)/N:y

L12 ANSWER 1 OF 5 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2008408883 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18390540  
TITLE: Brain-derived neurotrophic factor stimulates bone/cementum-related protein gene expression in cementoblasts.  
AUTHOR: Kajiyama Mikihitto; Shiba Hideki; Fujita Tsuyoshi; Ouhara Kazuhisa; Takeda Katsuhiro; Mizuno Noriyoshi; Kawaguchi Hiroyuki; Kitagawa Masaë; Takata Takashi; Tsuji Koichiro; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Hiroshima University Graduate School of Biomedical Sciences, Minami-ku, Hiroshima 34-8553, Japan.  
SOURCE: The Journal of biological chemistry, (2008 Jun 6) Vol. 283, No. 23, pp. 16259-67. Electronic Publication: 2008-04-03. Journal code: 2985121R. ISSN: 0021-9258.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English

FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200807  
ENTRY DATE: Entered STN: 27 Jun 2008  
Last Updated on STN: 16 Jul 2008  
Entered Medline: 15 Jul 2008  
AB Brain-derived neurotrophic factor (BDNF), recognized as essential in the developing nervous system, is involved in differentiation and proliferation in non-neuronal cells, such as endothelial cells, osteoblasts, and periodontal ligament cells. We have focused on the application of BDNF to the regeneration of periodontal tissue and indicated that BDNF promotes the regeneration of experimentally created periodontal defects. Cementoblasts form cementum, mineralized tissue, which is key to establishing functional periodontium. The application of BDNF to the regeneration of periodontal tissue requires elucidation of the mechanism by which BDNF regulates the functions of cementoblasts. In this study, we examined how BDNF regulates the mRNA expression of bone/cementum-related proteins (alkaline phosphatase (ALP), osteopontin (OPN), and bone morphogenetic protein-2 (BMP-2)) in cultures of immortalized human cementoblast-like (HCEM) cells. BDNF elevated the mRNA levels of ALP, OPN, and BMP-2 in HCEM cells. Small interfering RNA (siRNA) for TRKB, a high affinity receptor of BDNF, siRNA for ELK-1, which is a downstream target of ERK1/2, and PD98059, an ERK inhibitor, obviated the increase in the mRNA levels. BDNF increased the levels of phosphorylated ERK1/2 and Elk-1, and the blocking of BDNF signaling by treatment with siRNA for TRKB and PD98059 suppressed the phosphorylation of ERK1/2 and Elk-1. Furthermore, BDNF increased the levels of phosphorylated c-Raf, which activates the ERK signaling pathway. These findings provide the first evidence that the TrkB-c-Raf-ERK1/2-Elk-1 signaling pathway is required for the BDNF-induced mRNA expression of ALP, OPN, and BMP-2 in HCEM cells.

L12 ANSWER 2 OF 5 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2008714203 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18980528  
TITLE: Effect of neurotrophin-4/5 on bone/cementum-related protein expressions and DNA synthesis in cultures of human periodontal ligament cells.  
AUTHOR: Mizuno Noriyoshi; Shiba Hideki; Inui Takafumi; Takeda Katsuhiko; Kajiya Mikihitto; Hasegawa Naohiko; Kawaguchi Hiroyuki; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.. mizuno@hiroshima-u.ac.jp  
SOURCE: Journal of periodontology, (2008 Nov) Vol. 79, No. 11, pp. 2182-9.  
Journal code: 8000345. ISSN: 0022-3492.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOVT)  
LANGUAGE: English  
FILE SEGMENT: Dental Journals; Priority Journals  
ENTRY MONTH: 200902  
ENTRY DATE: Entered STN: 5 Nov 2008  
Last Updated on STN: 15 Feb 2009  
Entered Medline: 12 Feb 2009

AB BACKGROUND: We studied neurotrophins (NTs) as signaling molecules for periodontal tissue regeneration and showed that nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) modulate the proliferation and differentiation of human periodontal ligament (HPL) cells in vitro. The purpose of this study was to investigate whether NT-4/5 also has the ability to regulate the function of HPL cells. METHODS: mRNA expressions of NT-4/5 and its

high-affinity tyrosine kinase receptor (trkB) were analyzed in HPL cells by reverse transcription-polymerase chain reaction. We examined how NT-4/5 regulates the mRNA expression of bone/cementum-related proteins (alkaline phosphatase [ALPase], osteopontin [OPN], osteocalcin [OC], and bone morphogenetic protein [BMP]-2) in cultures of HPL cells. Moreover, the effects of NT-4/5 on calcification, the production of OPN and OC, and DNA synthesis in HPL cells were examined. RESULTS: NT-4/5 and trkB mRNA were expressed in HPL cells. NT-4/5 elevated the mRNA levels of ALPase, OPN, OC, and BMP-2 and the syntheses of OPN, OC, and DNA in HPL cells. PD98059, an extracellular signal-regulated kinase (ERK) inhibitor, obviated the increase in the mRNA levels of ALPase, OPN, OC, and BMP-2. NT-4/5 increased the levels of phosphorylated ERK1/2. Furthermore, NT-4/5 enhanced the amount of mineral deposits in cultures of HPL cells. CONCLUSION: NT-4/5, as well as BDNF and NGF, is suggested to play a role in the regulation of function of periodontal ligament cells.

L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2005:259902 CAPLUS

DOCUMENT NUMBER: 142:303690  
TITLE: Remedy and therapeutic method for periodontal diseases and pulpal diseases with neurotrophic factors

INVENTOR(S): Kurihara, Hidemi; Kawaguchi, Hiroyuki; Takeda, Katsuhiro; Shiba, Hideki; Mizuno, Noriyoshi; Yoshino, Hiroshi; Hasegawa, Naohiko; Shinohara, Hiroaki  
PATENT ASSIGNEE(S): Two Cells Co. Ltd., Japan  
SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025605	A1	20050324	WO 2004-JP13023	20040908
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TT, TZ, UA, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004271843	A1	20050324	AU 2004-271843	20040908
EP 1671641	A1	20060621	EP 2004-787706	20040908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1871024	A	20061129	CN 2004-80031194	20040908
RU 2336089	C2	20081020	RU 2006-111465	20040908
US 20070071693	A1	20070329	US 2006-571069	20061207
PRIORITY APPLN. INFO.:			JP 2003-316719 WO 2004-JP13023	A 20030909 W 20040908

AB It is intended to provide a remedy and a therapeutic method for periodontal diseases and pulpal diseases, a transplantation material for regenerating a periodontal tissue and a method of regenerating a periodontal tissue. Namely, a remedy for periodontal diseases and pulpal diseases comprising a

neurotrophic factor as the active ingredient. The effect of brain-derived neurotrophic factor (BDNF) on cultured human periodontal ligament cell and human gingival keratinocyte was examined

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 5 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 2005583578 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 16259615  
TITLE: Brain-derived neurotrophic factor enhances periodontal tissue regeneration.  
AUTHOR: Takeda Katsuhiko; Shiba Hideki; Mizuno Noriyoshi; Hasegawa Naohiko; Mouri Yoshihiro; Hirachi Akio; Yoshino Hiroshi; Kawaguchi Hiroyuki; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.  
SOURCE: Tissue engineering, (2005 Sep-Oct) Vol. 11, No. 9-10, pp. 1618-29.  
Journal code: 9505538. ISSN: 1076-3279.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (COMPARATIVE STUDY)  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200512  
ENTRY DATE: Entered STN: 3 Nov 2005  
Last Updated on STN: 23 Dec 2005  
Entered Medline: 22 Dec 2005

AB To address whether brain-derived neurotrophic factor (BDNF) could be involved in periodontal tissue regeneration, we examined the effects of BDNF on proliferation and the expression of bone (cementum)- related proteins (osteopontin, bone morphogenetic protein [BMP]-2, type I collagen, alkaline phosphatase [ALPase], and osteocalcin) in cultures of human periodontal ligament (HPL) cells, which are thought to be prerequisite for periodontal tissue regeneration, and on proliferation and angiogenesis in human endothelial cells. Furthermore, we examined the effect of BDNF on the regeneration of periodontal tissues in experimentally induced periodontal defects in dogs. BDNF elevated the expression of ALPase and osteocalcin mRNAs and increased the synthesis of osteopontin, BMP-2, and type I collagen DNA in HPL cells. BDNF stimulated mRNA expression of vascular endothelial growth factor-B and tenascin-X, and proliferation and angiogenesis in human endothelial cells. In vivo studies showed that BDNF stimulated the formation of new alveolar bone cementum and connective new fibers, which were inserted into the newly formed cementum and bone. BDNF also stimulated blood capillary formation. These findings suggest that the regulation of functioning of periodontal ligament cells and endothelial cells by BDNF results in the promotion of periodontal tissue regeneration.

L12 ANSWER 5 OF 5 MEDLINE on STN DUPLICATE 4  
ACCESSION NUMBER: 2003081727 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12593600  
TITLE: Neurotrophins in cultured cells from periodontal tissues.  
AUTHOR: Kurihara Hidemi; Shinohara Hiroaki; Yoshino Hiroshi; Takeda Katsuhiko; Shiba Hideki  
CORPORATE SOURCE: Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of

Biomedical Science, Hiroshima, Japan..  
hkuri@hiroshima-u.ac.jp  
SOURCE: Journal of periodontology, (2003 Jan) Vol. 74, No. 1, pp.  
76-84. Ref: 67  
Journal code: 8000345. ISSN: 0022-3492.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Dental Journals; Priority Journals  
ENTRY MONTH: 200305  
ENTRY DATE: Entered STN: 21 Feb 2003  
Last Updated on STN: 8 May 2003  
Entered Medline: 7 May 2003

AB We review the basic functions of neurotrophins and their receptors and discuss the expression and functions of neurotrophins and their specific receptors based on recent data using cultured cells from human periodontal tissues. Neurotrophins, nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and neurotrophin-3 (NT-3) play crucial roles in the differentiation and survival of neural cells. Neurotrophins activate 2 different receptor classes: the tropomyosin-related kinase (Trk) family of receptor tyrosine kinases (TrkA, TrkB, and TrkC) and the p75 receptor, a member of the tumor necrosis factor receptor superfamily. Neurotrophins regulate both cell death and cell survival through activations of Trk receptors and/or p75 neurotrophin receptor. It has been reported that neurotrophins are also produced from non-neuronal cells, such as leukocytes, osteoblasts, or fibroblasts, and act in many other ways on non-neuronal cells. Neurotrophin expression during bone fracture healing is especially interesting, and neurotrophins are now implicated in hard tissue regeneration. It is well known that neurotrophins and their receptors are expressed in tooth development. Recent studies have found that neurotrophins and Trk receptors are expressed in mouse osteoblastic cell lines. Human periodontal ligament cells, human gingival fibroblasts, and human gingival keratinocytes expressed mRNA for NGF and TrkA. The secretion of bioactive NGF peptides from human periodontal ligament cells and human gingival keratinocytes was confirmed by bioassay using PC12 cells (rat adrenal pheochromocytoma cells). The expression of NGF and TrkA mRNA was regulated by interleukin (IL)-1beta. NGF increased DNA synthesis and expressions of mRNA for bone-related proteins, alkaline phosphatase, and osteopontin in human periodontal ligament cells. Neurotrophins and Trk receptors expressed in human periodontal tissue may contribute to regeneration as well as innervation of periodontal tissue through local autocrine and paracrine pathways. Recent data suggest that some functions of neurotrophins and Trk receptors relate to periodontal disease and periodontal tissue regeneration. However, *in vivo* studies will be required to clarify the roles of neurotrophins and their receptors, including p75, in periodontal disease and periodontal tissue regeneration.

=> dis ibib abs 116 1-5

YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, CAPLUS' - CONTINUE? (Y)/N:y

ACCESSION NUMBER: 2008408883 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18390540  
TITLE: Brain-derived neurotrophic factor stimulates bone/cementum-related protein gene expression in cementoblasts.  
AUTHOR: Kajiya Mikihito; Shiba Hideki; Fujita Tsuyoshi; Ouhara Kazuhisa; Takeda Katsuhiro; Mizuno Noriyoshi; Kawaguchi Hiroyuki; Kitagawa Masaë; Takata Takashi; Tsuji Koichiro; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Hiroshima University Graduate School of Biomedical Sciences, Minami-ku, Hiroshima 34-8553, Japan.  
SOURCE: The Journal of biological chemistry, (2008 Jun 6) Vol. 283, No. 23, pp. 16259-67. Electronic Publication: 2008-04-03. Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200807

ENTRY DATE: Entered STN: 27 Jun 2008  
Last Updated on STN: 16 Jul 2008  
Entered Medline: 15 Jul 2008

**AB** Brain-derived neurotrophic factor (BDNF), recognized as essential in the developing nervous system, is involved in differentiation and proliferation in non-neuronal cells, such as endothelial cells, osteoblasts, and periodontal ligament cells. We have focused on the application of BDNF to the regeneration of periodontal tissue and indicated that BDNF promotes the regeneration of experimentally created periodontal defects. Cementoblasts form cementum, mineralized tissue, which is key to establishing a functional periodontium. The application of BDNF to the regeneration of periodontal tissue requires elucidation of the mechanism by which BDNF regulates the functions of cementoblasts. In this study, we examined how BDNF regulates the mRNA expression of bone/cementum-related proteins (alkaline phosphatase (ALP), osteopontin (OPN), and bone morphogenetic protein-2 (BMP-2) in cultures of immortalized human cementoblast-like (HCEM) cells. BDNF elevated the mRNA levels of ALP, OPN, and BMP-2 in HCEM cells. Small interfering RNA (siRNA) for TRKB, a high affinity receptor of BDNF, siRNA for ELK-1, which is a downstream target of ERK1/2, and PD98059, an ERK inhibitor, obviated the increase in the mRNA levels. BDNF increased the levels of phosphorylated ERK1/2 and Elk-1, and the blocking of BDNF signaling by treatment with siRNA for TRKB and PD98059 suppressed the phosphorylation of ERK1/2 and Elk-1. Furthermore, BDNF increased the levels of phosphorylated c-Raf, which activates the ERK signaling pathway. These findings provide the first evidence that the TrkB-c-Raf-ERK1/2-Elk-1 signaling pathway is required for the BDNF-induced mRNA expression of ALP, OPN, and BMP-2 in HCEM cells.

L16 ANSWER 2 OF 5 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2008714203 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18980528  
TITLE: Effect of neurotrophin-4/5 on bone/cementum-related protein expressions and DNA synthesis in cultures of human periodontal ligament cells.  
AUTHOR: Mizuno Noriyoshi; Shiba Hideki; Inui Takafumi; Takeda Katsuhiro; Kajiya Mikihito; Hasegawa Naohiko; Kawaguchi Hiroyuki; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.. mizuno@hiroshima-u.ac.jp

SOURCE: Journal of periodontology, (2008 Nov) Vol. 79, No. 11, pp. 2182-9.  
Journal code: 8000345. ISSN: 0022-3492.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Dental Journals; Priority Journals  
ENTRY MONTH: 200902  
ENTRY DATE: Entered STN: 5 Nov 2008  
Last Updated on STN: 15 Feb 2009  
Entered Medline: 12 Feb 2009

AB BACKGROUND: We studied neurotrophins (NTs) as signaling molecules for periodontal tissue regeneration and showed that nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) modulate the proliferation and differentiation of human periodontal ligament (HPL) cells in vitro. The purpose of this study was to investigate whether NT-4/5 also has the ability to regulate the function of HPL cells. METHODS: mRNA expressions of NT-4/5 and its high-affinity tyrosine kinase receptor (trkB) were analyzed in HPL cells by reverse transcription-polymerase chain reaction. We examined how NT-4/5 regulates the mRNA expression of bone/cementum-related proteins (alkaline phosphatase [ALPase], osteopontin [OPN], osteocalcin [OC], and bone morphogenetic protein [BMP]-2) in cultures of HPL cells. Moreover, the effects of NT-4/5 on calcification, the production of OPN and OC, and DNA synthesis in HPL cells were examined. RESULTS: NT-4/5 and trkB mRNA were expressed in HPL cells. NT-4/5 elevated the mRNA levels of ALPase, OPN, OC, and BMP-2 and the syntheses of OPN, OC, and DNA in HPL cells. PD98059, an extracellular signal-regulated kinase (ERK) inhibitor, obviated the increase in the mRNA levels of ALPase, OPN, OC, and BMP-2. NT-4/5 increased the levels of phosphorylated ERK1/2. Furthermore, NT-4/5 enhanced the amount of mineral deposits in cultures of HPL cells. CONCLUSION: NT-4/5, as well as BDNF and NGF, is suggested to play a role in the regulation of function of periodontal ligament cells.

L16 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:259902 CAPLUS

DOCUMENT NUMBER: 142:303690

TITLE: Remedy and therapeutic method for periodontal diseases and pulpal diseases with neurotrophic factors

INVENTOR(S): Kurihara, Hidemi; Kawaguchi, Hiroyuki; Takeda, Katsuhiro; Shiba, Hideki; Mizuno, Noriyoshi; Yoshino, Hiroshi; Hasegawa, Naohiko; Shinohara, Hiroaki

PATENT ASSIGNEE(S): Two Cells Co. Ltd., Japan

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025605	A1	20050324	WO 2004-JP13023	20040908
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004271843 A1 20050324 AU 2004-271843 20040908

EP 1671641 A1 20060621 EP 2004-787706 20040908

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

CN 1871024 A 20061129 CN 2004-80031194 20040908

RU 2336089 C2 20081020 RU 2006-111465 20040908

US 20070071693 A1 20070329 US 2006-571069 20061207

PRIORITY APPLN. INFO.: JP 2003-316719 A 20030909  
WO 2004-JP13023 W 20040908

AB It is intended to provide a remedy and a therapeutic method for periodontal diseases and pulpal diseases, a transplantation material for regenerating a periodontal tissue and a method of regenerating a periodontal tissue. Namely, a remedy for periodontal diseases and pulpal diseases comprising a neurotrophic factor as the active ingredient. The effect of brain-derived neurotrophic factor (BDNF) on cultured human periodontal ligament cell and human gingival keratinocyte was examined

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 5 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 2005583578 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 16259615  
TITLE: Brain-derived neurotrophic factor enhances periodontal tissue regeneration.  
AUTHOR: Takeda Katsuhiro; Shiba Hideki; Mizuno Noriyoshi; Hasegawa Naohiko; Mouri Yoshihiro; Hirachi Akio; Yoshino Hiroshi; Kawaguchi Hiroyuki; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.  
SOURCE: Tissue engineering, (2005 Sep-Oct) Vol. 11, No. 9-10, pp. 1618-29.  
Journal code: 9505538. ISSN: 1076-3279.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (COMPARATIVE STUDY)  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200512  
ENTRY DATE: Entered STN: 3 Nov 2005  
Last Updated on STN: 23 Dec 2005  
Entered Medline: 22 Dec 2005

AB To address whether brain-derived neurotrophic factor (BDNF) could be involved in periodontal tissue regeneration, we examined the effects of BDNF on proliferation and the expression of bone (cementum)- related proteins (osteopontin, bone morphogenetic protein [BMP]-2, type I collagen, alkaline phosphatase [ALPase], and osteocalcin) in cultures of human periodontal ligament (HPL) cells, which are thought to be prerequisite for periodontal tissue regeneration, and on proliferation and angiogenesis in human endothelial cells. Furthermore, we examined the effect of BDNF on the regeneration of periodontal tissues in experimentally induced periodontal defects in dogs. BDNF elevated the expression of ALPase and osteocalcin mRNAs and increased the synthesis of osteopontin, BMP-2, and type I

collagen DNA in HPL cells. BDNF stimulated mRNA expression of vascular endothelial growth factor-B and tenascin-X, and proliferation and angiogenesis in human endothelial cells. *In vivo* studies showed that BDNF stimulated the formation of new alveolar bone cementum and connective new fibers, which were inserted into the newly formed cementum and bone. BDNF also stimulated blood capillary formation. These findings suggest that the regulation of functioning of periodontal ligament cells and endothelial cells by BDNF results in the promotion of periodontal tissue regeneration.

L16 ANSWER 5 OF 5 MEDLINE on STN DUPPLICATE 4  
 ACCESSION NUMBER: 2003081727 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 12593600  
 TITLE: Neurotrophins in cultured cells from periodontal tissues.  
 AUTHOR: Kurihara Hideki; Shinohara Hiroaki; Yoshino Hiroshi; Takeda Katsuhiro; Shiba Hideki  
 CORPORATE SOURCE: Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of Biomedical Science, Hiroshima, Japan..  
 SOURCE: hkurii@hiroshima-u.ac.jp  
 Journal of periodontology, (2003 Jan) Vol. 74, No. 1, pp. 76-84. Ref: 67  
 PUB. COUNTRY: Journal code: 8000345. ISSN: 0022-3492.  
 DOCUMENT TYPE: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 General Review; (REVIEW)  
 LANGUAGE: English  
 FILE SEGMENT: Dental Journals; Priority Journals  
 ENTRY MONTH: 200305  
 ENTRY DATE: Entered STN: 21 Feb 2003  
 Last Updated on STN: 8 May 2003  
 Entered Medline: 7 May 2003

AB We review the basic functions of neurotrophins and their receptors and discuss the expression and functions of neurotrophins and their specific receptors based on recent data using cultured cells from human periodontal tissues. Neurotrophins, nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and neurotrophin-3 (NT-3) play crucial roles in the differentiation and survival of neural cells. Neurotrophins activate 2 different receptor classes: the tropomyosin-related kinase (Trk) family of receptor tyrosine kinases (TrkA, TrkB, and TrkC) and the p75 receptor, a member of the tumor necrosis factor receptor superfamily. Neurotrophins regulate both cell death and cell survival through activations of Trk receptors and/or p75 neurotrophin receptor. It has been reported that neurotrophins are also produced from non-neuronal cells, such as leukocytes, osteoblasts, or fibroblasts, and act in many other ways on non-neuronal cells. Neurotrophin expression during bone fracture healing is especially interesting, and neurotrophins are now implicated in hard tissue regeneration. It is well known that neurotrophins and their receptors are expressed in tooth development. Recent studies have found that neurotrophins and Trk receptors are expressed in mouse osteoblastic cell lines. Human periodontal ligament cells, human gingival fibroblasts, and human gingival keratinocytes expressed mRNA for NGF and TrkA. The secretion of bioactive NGF peptides from human periodontal ligament cells and human gingival keratinocytes was confirmed by bioassay using PC12 cells (rat adrenal pheochromocytoma cells). The expression of NGF and TrkA mRNA was regulated by interleukin (IL)-1beta. NGF increased DNA synthesis and expressions of mRNA for bone-related proteins, alkaline phosphatase, and

osteopontin in human periodontal ligament cells. Neurotrophins and Trk receptors expressed in human periodontal tissue may contribute to regeneration as well as innervation of periodontal tissue through local autocrine and paracrine pathways. Recent data suggest that some functions of neurotrophins and Trk receptors relate to periodontal disease and periodontal tissue regeneration. However, *in vivo* studies will be required to clarify the roles of neurotrophins and their receptors, including p75, in periodontal disease and periodontal tissue regeneration.

=> dis ibib abs l20 1-4  
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, CAPLUS' - CONTINUE? (Y)/N:y

L20 ANSWER 1 OF 4 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2008408883 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18390540  
TITLE: Brain-derived neurotrophic factor stimulates bone/cementum-related protein gene expression in cementoblasts.  
AUTHOR: Kajiya Mikihito; Shiba Hideki; Fujita Tsuyoshi; Ohara Kazuhisa; Takeda Katsuhiro; Mizuno Noriyoshi; Kawaguchi Hiroyuki; Kitagawa Masaee; Takata Takashi; Tsuji Koichiro; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Hiroshima University Graduate School of Biomedical Sciences, Minami-ku, Hiroshima 34-8553, Japan.  
SOURCE: The Journal of biological chemistry, (2008 Jun 6) Vol. 283, No. 23, pp. 16259-67. Electronic Publication: 2008-04-03. Journal code: 2985121R. ISSN: 0021-9258.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200807  
ENTRY DATE: Entered STN: 27 Jun 2008  
Last Updated on STN: 16 Jul 2008  
Entered Medline: 15 Jul 2008  
AB Brain-derived neurotrophic factor (BDNF), recognized as essential in the developing nervous system, is involved in differentiation and proliferation in non-neuronal cells, such as endothelial cells, osteoblasts, and periodontal ligament cells. We have focused on the application of BDNF to the regeneration of periodontal tissue and indicated that BDNF promotes the regeneration of experimentally created periodontal defects. Cementoblasts form cementum, mineralized tissue, which is key to establishing a functional periodontium. The application of BDNF to the regeneration of periodontal tissue requires elucidation of the mechanism by which BDNF regulates the functions of cementoblasts. In this study, we examined how BDNF regulates the mRNA expression of bone/cementum-related proteins (alkaline phosphatase (ALP), osteopontin (OPN), and bone morphogenetic protein-2 (BMP-2)) in cultures of immortalized human cementoblast-like (HCEM) cells. BDNF elevated the mRNA levels of ALP, OPN, and BMP-2 in HCEM cells. Small interfering RNA (siRNA) for TRKB, a high affinity receptor of BDNF, siRNA for ELK-1, which is a downstream target of ERK1/2, and PD98059, an ERK inhibitor, obviated the increase in the mRNA levels. BDNF increased the levels of phosphorylated ERK1/2 and Elk-1, and the

blocking of BDNF signaling by treatment with siRNA for TRKB and PD98059 suppressed the phosphorylation of ERK1/2 and Elk-1. Furthermore, BDNF increased the levels of phosphorylated c-Raf, which activates the ERK signaling pathway. These findings provide the first evidence that the TrkB-c-Raf-ERK1/2-Elk-1 signaling pathway is required for the BDNF-induced mRNA expression of ALP, OPN, and BMP-2 in HCEM cells.

L20 ANSWER 2 OF 4 MEDLINE on STN DUPPLICATE 2  
ACCESSION NUMBER: 2008714203 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18980528  
TITLE: Effect of neurotrophin-4/5 on bone/cementum-related protein expressions and DNA synthesis in cultures of human periodontal ligament cells.  
AUTHOR: Mizuno Noriyoshi; Shiba Hideki; Inui Takafumi; Takeda Katsuhiro; Kajiya Mikihito; Hasegawa Naohiko; Kawaguchi Hiroyuki; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.. mizuno@hiroshima-u.ac.jp  
SOURCE: Journal of periodontology, (2008 Nov) Vol. 79, No. 11, pp. 2182-9.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Dental Journals; Priority Journals  
ENTRY MONTH: 200902  
ENTRY DATE: Entered STN: 5 Nov 2008  
Last Updated on STN: 15 Feb 2009  
Entered Medline: 12 Feb 2009  
AB BACKGROUND: We studied neurotrophins (NTs) as signaling molecules for periodontal tissue regeneration and showed that nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) modulate the proliferation and differentiation of human periodontal ligament (HPL) cells in vitro. The purpose of this study was to investigate whether NT-4/5 also has the ability to regulate the function of HPL cells. METHODS: mRNA expressions of NT-4/5 and its high-affinity tyrosine kinase receptor (trkB) were analyzed in HPL cells by reverse transcription-polymerase chain reaction. We examined how NT-4/5 regulates the mRNA expression of bone/cementum-related proteins (alkaline phosphatase [ALPase], osteopontin [OPN], osteocalcin [OC], and bone morphogenetic protein [BMP]-2) in cultures of HPL cells. Moreover, the effects of NT-4/5 on calcification, the production of OPN and OC, and DNA synthesis in HPL cells were examined. RESULTS: NT-4/5 and trkB mRNA were expressed in HPL cells. NT-4/5 elevated the mRNA levels of ALPase, OPN, OC, and BMP-2 and the syntheses of OPN, OC, and DNA in HPL cells. PD98059, an extracellular signal-regulated kinase (ERK) inhibitor, obviated the increase in the mRNA levels of ALPase, OPN, OC, and BMP-2. NT-4/5 increased the levels of phosphorylated ERK1/2. Furthermore, NT-4/5 enhanced the amount of mineral deposits in cultures of HPL cells. CONCLUSION: NT-4/5, as well as BDNF and NGF, is suggested to play a role in the regulation of function of periodontal ligament cells.

L20 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2005:259902 CAPLUS  
DOCUMENT NUMBER: 1421:303690  
TITLE: Remedy and therapeutic method for periodontal diseases and pulpal diseases with neurotrophic factors  
INVENTOR(S): Kurihara, Hidemi; Kawaguchi, Hiroyuki; Takeda, Katsuhiro; Shiba, Hideki; Mizuno, Noriyoshi;

Yoshino, Hiroshi; Hasegawa, Naohiko; Shinohara, Hiroaki  
 PATENT ASSIGNEE(S): Two Cells Co. Ltd., Japan  
 SOURCE: PCT Int. Appl., 86 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 200502605	A1	20050324	WO 2004-JP13023	20040908
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004271843	A1	20050324	AU 2004-271843	20040908
EP 1671641	A1	20060621	EP 2004-787706	20040908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1871024	A	20061129	CN 2004-80031194	20040908
RU 2336089	C2	20081020	RU 2006-111465	20040908
US 20070071693	A1	20070329	US 2006-571069	20061207
PRIORITY APPLN. INFO.:			JP 2003-316719	A 20030909
			WO 2004-JP13023	W 20040908

**AB** It is intended to provide a remedy and a therapeutic method for periodontal diseases and pulpal diseases, a transplantation material for regenerating a periodontal tissue and a method of regenerating a periodontal tissue. Namely, a remedy for periodontal diseases and pulpal diseases comprising a neurotrophic factor as the active ingredient. The effect of brain-derived neurotrophic factor (BDNF) on cultured human periodontal ligament cell and human gingival keratinocyte was examined

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 3  
 ACCESSION NUMBER: 2005583578 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 16259615  
 TITLE: Brain-derived neurotrophic factor enhances periodontal tissue regeneration.  
 AUTHOR: Takeda Katsuhiro; Shiba Hideki; Mizuno Noriyoshi; Hasegawa Naohiko; Mouri Yoshihiro; Hirachi Akio; Yoshino Hiroshi; Kawaguchi Hiroyuki; Kurihara Hidemi  
 CORPORATE SOURCE: Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.  
 SOURCE: Tissue engineering, (2005 Sep-Oct) Vol. 11, No. 9-10, pp. 1618-29.  
 Journal code: 9505538. ISSN: 1076-3279.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: (COMPARATIVE STUDY)  
 Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200512  
ENTRY DATE: Entered STN: 3 Nov 2005  
Last Updated on STN: 23 Dec 2005  
Entered Medline: 22 Dec 2005

AB To address whether brain-derived neurotrophic factor (BDNF) could be involved in periodontal tissue regeneration, we examined the effects of BDNF on proliferation and the expression of bone (cementum)- related proteins (osteopontin, bone morphogenetic protein [BMP]-2, type I collagen, alkaline phosphatase [ALPase], and osteocalcin) in cultures of human periodontal ligament (HPL) cells, which are thought to be prerequisite for periodontal tissue regeneration, and on proliferation and angiogenesis in human endothelial cells. Furthermore, we examined the effect of BDNF on the regeneration of periodontal tissues in experimentally induced periodontal defects in dogs. BDNF elevated the expression of ALPase and osteocalcin mRNAs and increased the synthesis of osteopontin, BMP-2, and type I collagen DNA in HPL cells. BDNF stimulated mRNA expression of vascular endothelial growth factor-B and tenascin-X, and proliferation and angiogenesis in human endothelial cells. In vivo studies showed that BDNF stimulated the formation of new alveolar bone cementum and connective new fibers, which were inserted into the newly formed cementum and bone. BDNF also stimulated blood capillary formation. These findings suggest that the regulation of functioning of periodontal ligament cells and endothelial cells by BDNF results in the promotion of periodontal tissue regeneration.

=> dis ibib abs l24 1-3

YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, CAPLUS' - CONTINUE? (Y)/N:y

L24 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2005:259902 CAPLUS  
DOCUMENT NUMBER: 142:303690  
TITLE: Remedy and therapeutic method for periodontal diseases and pulpal diseases with neurotrophic factors  
INVENTOR(S): Kurihara, Hidemi; Kawaguchi, Hiroyuki; Takeda, Katsuhiro; Shiba, Hideki; Mizuno, Noriyoshi; Yoshino, Hiroshi; Hasegawa, Naohiko; Shinohara, Hiroaki  
PATENT ASSIGNEE(S): Two Cells Co. Ltd., Japan  
SOURCE: PCT Int. Appl., 86 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025605	A1	20050324	WO 2004-JP13023	20040908
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
SN, TD, TG

AU 2004271843	A1	20050324	AU 2004-271843	20040908
EP 1671641	A1	20060621	EP 2004-787706	20040908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1871024	A	20061129	CN 2004-80031194	20040908
RU 2336089	C2	20081020	RU 2006-111465	20040908
US 20070071693	A1	20070329	US 2006-571069	20061207
PRIORITY APPLN. INFO.:			JP 2003-316719	A 20030909
			WO 2004-JP13023	W 20040908

AB It is intended to provide a remedy and a therapeutic method for periodontal diseases and pulpal diseases, a transplantation material for regenerating a periodontal tissue and a method of regenerating a periodontal tissue. Namely, a remedy for periodontal diseases and pulpal diseases comprising a neurotrophic factor as the active ingredient. The effect of brain-derived neurotrophic factor (BDNF) on cultured human periodontal ligament cell and human gingival keratinocyte was examined

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2005583578 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 16259615  
TITLE: Brain-derived neurotrophic factor enhances periodontal tissue regeneration.  
AUTHOR: Takeda Katsuhiro; Shiba Hideki; Mizuno Noriyoshi; Hasegawa Naoko; Mouri Yoshihiro; Hirachi Akio; Yoshino Hiroshi; Kawaguchi Hiroyuki; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.  
SOURCE: Tissue engineering, (2005 Sep-Oct) Vol. 11, No. 9-10, pp. 1618-29.  
JOURNAL CODE: 9505538. ISSN: 1076-3279.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (COMPARATIVE STUDY)  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200512  
ENTRY DATE: Entered STN: 3 Nov 2005  
Last Updated on STN: 23 Dec 2005  
Entered Medline: 22 Dec 2005

AB To address whether brain-derived neurotrophic factor (BDNF) could be involved in periodontal tissue regeneration, we examined the effects of BDNF on proliferation and the expression of bone (cementum)- related proteins (osteopontin, bone morphogenetic protein [BMP]-2, type I collagen, alkaline phosphatase [ALPase], and osteocalcin) in cultures of human periodontal ligament (HPL) cells, which are thought to be prerequisite for periodontal tissue regeneration, and on proliferation and angiogenesis in human endothelial cells. Furthermore, we examined the effect of BDNF on the regeneration of periodontal tissues in experimentally induced periodontal defects in dogs. BDNF elevated the expression of ALPase and osteocalcin

mRNAs and increased the synthesis of osteopontin, BMP-2, and type I collagen DNA in HPL cells. BDNF stimulated mRNA expression of vascular endothelial growth factor-B and tenascin-X, and proliferation and angiogenesis in human endothelial cells. In vivo studies showed that BDNF stimulated the formation of new alveolar bone cementum and connective new fibers, which were inserted into the newly formed cementum and bone. BDNF also stimulated blood capillary formation. These findings suggest that the regulation of functioning of periodontal ligament cells and endothelial cells by BDNF results in the promotion of periodontal tissue regeneration.

L24 ANSWER 3 OF 3      MEDLINE on STN      DUPLICATE 2  
ACCESSION NUMBER: 2003081727      MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12593600  
TITLE:      Neurotrophins in cultured cells from periodontal tissues.  
AUTHOR:      Kurihara Hidemi; Shinohara Hiroaki; Yoshino Hiroshi ; Takeda Katsuhiro; Shiba Hideki  
CORPORATE SOURCE:      Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of Biomedical Science, Hiroshima, Japan.. hkuri@hiroshima-u.ac.jp  
SOURCE:      Journal of periodontology, (2003 Jan) Vol. 74, No. 1, pp. 76-84. Ref: 67  
                 Journal code: 8000345. ISSN: 0022-3492.  
PUB. COUNTRY:      United States  
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)  
                 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
                 General Review; (REVIEW)  
LANGUAGE:      English  
FILE SEGMENT:      Dental Journals; Priority Journals  
ENTRY MONTH:      200305  
ENTRY DATE:      Entered STN: 21 Feb 2003  
                 Last Updated on STN: 8 May 2003  
                 Entered Medline: 7 May 2003

AB      We review the basic functions of neurotrophins and their receptors and discuss the expression and functions of neurotrophins and their specific receptors based on recent data using cultured cells from human periodontal tissues. Neurotrophins, nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and neurotrophin-3 (NT-3) play crucial roles in the differentiation and survival of neural cells. Neurotrophins activate 2 different receptor classes: the tropomyosin-related kinase (Trk) family of receptor tyrosine kinases (TrkA, TrkB, and TrkC) and the p75 receptor, a member of the tumor necrosis factor receptor superfamily. Neurotrophins regulate both cell death and cell survival through activations of Trk receptors and/or p75 neurotrophin receptor. It has been reported that neurotrophins are also produced from non-neuronal cells, such as leukocytes, osteoblasts, or fibroblasts, and act in many other ways on non-neuronal cells. Neurotrophin expression during bone fracture healing is especially interesting, and neurotrophins are now implicated in hard tissue regeneration. It is well known that neurotrophins and their receptors are expressed in tooth development. Recent studies have found that neurotrophins and Trk receptors are expressed in mouse osteoblastic cell lines. Human periodontal ligament cells, human gingival fibroblasts, and human gingival keratinocytes expressed mRNA for NGF and TrkA. The secretion of bioactive NGF peptides from human periodontal ligament cells and human gingival keratinocytes was confirmed by bioassay using PC12 cells (rat adrenal pheochromocytoma cells). The expression of NGF and TrkA mRNA was regulated by interleukin (IL)-1beta. NGF increased DNA synthesis and

expressions of mRNA for bone-related proteins, alkaline phosphatase, and osteopontin in human periodontal ligament cells. Neurotrophins and Trk receptors expressed in human periodontal tissue may contribute to regeneration as well as innervation of periodontal tissue through local autocrine and paracrine pathways. Recent data suggest that some functions of neurotrophins and Trk receptors relate to periodontal disease and periodontal tissue regeneration. However, *in vivo* studies will be required to clarify the roles of neurotrophins and their receptors, including p75, in periodontal disease and periodontal tissue regeneration.

=> dis ibib abs l28 1-3

YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, CAPLUS' - CONTINUE? (Y/N:y

L28 ANSWER 1 OF 3 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2008714203 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18980528  
TITLE: Effect of neurotrophin-4/5 on bone/cementum-related protein expressions and DNA synthesis in cultures of human periodontal ligament cells.  
AUTHOR: Mizuno Noriyoshi; Shiba Hideki; Inui Takafumi; Takeda Katsuhiko; Kajiya Mikihitto; Hasegawa Naohiko; Kawaguchi Hiroyuki; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.. mizuno@hiroshima-u.ac.jp  
SOURCE: Journal of periodontology, (2008 Nov) Vol. 79, No. 11, pp. 2182-9.  
PUB. COUNTRY: Journal code: 8000345. ISSN: 0022-3492.  
DOCUMENT TYPE: United States  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Dental Journals; Priority Journals  
ENTRY MONTH: 200902  
ENTRY DATE: Entered STN: 5 Nov 2008  
Last Updated on STN: 15 Feb 2009  
Entered Medline: 12 Feb 2009  
AB BACKGROUND: We studied neurotrophins (NTs) as signaling molecules for periodontal tissue regeneration and showed that nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) modulate the proliferation and differentiation of human periodontal ligament (HPL) cells *in vitro*. The purpose of this study was to investigate whether NT-4/5 also has the ability to regulate the function of HPL cells. METHODS: mRNA expressions of NT-4/5 and its high-affinity tyrosine kinase receptor (trkB) were analyzed in HPL cells by reverse transcription-polymerase chain reaction. We examined how NT-4/5 regulates the mRNA expression of bone/cementum-related proteins (alkaline phosphatase [ALPase], osteopontin [OPN], osteocalcin [OC], and bone morphogenetic protein [BMP]-2) in cultures of HPL cells. Moreover, the effects of NT-4/5 on calcification, the production of OPN and OC, and DNA synthesis in HPL cells were examined. RESULTS: NT-4/5 and trkB mRNA were expressed in HPL cells. NT-4/5 elevated the mRNA levels of ALPase, OPN, OC, and BMP-2 and the syntheses of OPN, OC, and DNA in HPL cells. PD98059, an extracellular signal-regulated kinase (ERK) inhibitor, obviated the increase in the mRNA levels of ALPase, OPN, OC, and BMP-2. NT-4/5 increased the levels of phosphorylated ERK1/2. Furthermore, NT-4/5

enhanced the amount of mineral deposits in cultures of HPL cells.  
CONCLUSION: NT-4/5, as well as BDNF and NGF, is suggested to play a role  
in the regulation of function of periodontal ligament cells.

L28 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2005:259902 CAPLUS  
DOCUMENT NUMBER: 142:303690  
TITLE: Remedy and therapeutic method for periodontal  
diseases and pulpal diseases with neurotrophic  
factors  
INVENTOR(S): Kurihara, Hidemi; Kawaguchi, Hiroyuki; Takeda,  
Katsuhiro; Shiba, Hideki; Mizuno, Noriyoshi; Yoshino,  
Hiroshi; Hasegawa, Naohiko; Shinohara,  
Hiroaki  
PATENT ASSIGNEE(S): Two Cells Co. Ltd., Japan  
SOURCE: PCT Int. Appl., 86 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025605	A1	20050324	WO 2004-JP13023	20040908
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004271843	A1	20050324	AU 2004-271843	20040908
EP 1671641	A1	20060621	EP 2004-787706	20040908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1871024	A	20061129	CN 2004-80031194	20040908
RU 2336089	C2	20081020	RU 2006-111465	20040908
US 20070071693	A1	20070329	US 2006-571069	20061207
PRIORITY APPLN. INFO.:			JP 2003-316719	A 20030909
			WO 2004-JP13023	W 20040908

AB It is intended to provide a remedy and a therapeutic method for  
periodontal diseases and pulpal diseases, a transplantation  
material for regenerating a periodontal tissue and a method of  
regenerating a periodontal tissue. Namely, a remedy for  
periodontal diseases and pulpal diseases comprising a  
neurotrophic factor as the active ingredient. The effect of  
brain-derived neurotrophic factor (BDNF) on cultured human  
periodontal ligament cell and human gingival keratinocyte was  
examined

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2005583578 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 16259615  
TITLE: Brain-derived neurotrophic factor enhances  
periodontal tissue regeneration.

AUTHOR: Takeda Katsuhiro; Shiba Hideki; Mizuno Noriyoshi; Hasegawa Naohiko; Mouri Yoshihiro; Hirachi Akio; Yoshino Hiroshi; Kawaguchi Hiroyuki; Kurihara Hidemi  
CORPORATE SOURCE: Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.  
SOURCE: Tissue engineering, (2005 Sep-Oct) Vol. 11, No. 9-10, pp. 1618-29.  
Journal code: 9505538. ISSN: 1076-3279.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (COMPARATIVE STUDY)  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200512  
ENTRY DATE: Entered STN: 3 Nov 2005  
Last Updated on STN: 23 Dec 2005  
Entered Medline: 22 Dec 2005  
AB To address whether brain-derived neurotrophic factor (BDNF) could be involved in periodontal tissue regeneration, we examined the effects of BDNF on proliferation and the expression of bone (cementum)- related proteins (osteopontin, bone morphogenetic protein [BMP]-2, type I collagen, alkaline phosphatase [ALPase], and osteocalcin) in cultures of human periodontal ligament (HPL) cells, which are thought to be prerequisite for periodontal tissue regeneration, and on proliferation and angiogenesis in human endothelial cells. Furthermore, we examined the effect of BDNF on the regeneration of periodontal tissues in experimentally induced periodontal defects in dogs. BDNF elevated the expression of ALPase and osteocalcin mRNAs and increased the synthesis of osteopontin, BMP-2, and type I collagen DNA in HPL cells. BDNF stimulated mRNA expression of vascular endothelial growth factor-B and tenascin-X, and proliferation and angiogenesis in human endothelial cells. In vivo studies showed that BDNF stimulated the formation of new alveolar bone cementum and connective new fibers, which were inserted into the newly formed cementum and bone. BDNF also stimulated blood capillary formation. These findings suggest that the regulation of functioning of periodontal ligament cells and endothelial cells by BDNF results in the promotion of periodontal tissue regeneration.

=> dis ibib abs 132 1-2  
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, CAPLUS' - CONTINUE? (Y)/N:y

L32 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2005:259902 CAPLUS  
DOCUMENT NUMBER: 142:303690  
TITLE: Remedy and therapeutic method for periodontal diseases and pulpal diseases with neurotrophic factors  
INVENTOR(S): Kurihara, Hidemi; Kawaguchi, Hiroyuki; Takeda, Katsuhiro; Shiba, Hideki; Mizuno, Noriyoshi; Yoshino, Hiroshi; Hasegawa, Naohiko; Shinohara, Hiroaki  
PATENT ASSIGNEE(S): Two Cells Co. Ltd., Japan  
SOURCE: PCT Int. Appl., 86 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025605	A1	20050324	WO 2004-JP13023	20040908
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004271843	A1	20050324	AU 2004-271843	20040908
EP 1671641	A1	20060621	EP 2004-787706	20040908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1871024	A	20061129	CN 2004-80031194	20040908
RU 2336089	C2	20081020	RU 2006-111465	20040908
US 20070071693	A1	20070329	US 2006-571069	20061207

PRIORITY APPLN. INFO.:

AB It is intended to provide a remedy and a therapeutic method for periodontal diseases and pulpal diseases, a transplantation material for regenerating a periodontal tissue and a method of regenerating a periodontal tissue. Namely, a remedy for periodontal diseases and pulpal diseases comprising a neurotrophic factor as the active ingredient. The effect of brain-derived neurotrophic factor (BDNF) on cultured human periodontal ligament cell and human gingival keratinocyte was examined

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2003081727 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12593600  
TITLE: Neurotrophins in cultured cells from periodontal tissues.  
AUTHOR: Kurihara Hidemi; Shinohara Hiroaki; Yoshino Hiroshi; Takeda Katsuhiro; Shiba Hideki  
CORPORATE SOURCE: Department of Periodontal Medicine, Division of Frontier Medical Science, Hiroshima University Graduate School of Biomedical Science, Hiroshima, Japan..  
hkur@hiroshima-u.ac.jp  
SOURCE: Journal of periodontology, (2003 Jan) Vol. 74, No. 1, pp. 76-84. Ref: 67  
Journal code: 8000345. ISSN: 0022-3492.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Dental Journals; Priority Journals  
ENTRY MONTH: 200305  
ENTRY DATE: Entered STN: 21 Feb 2003  
Last Updated on STN: 8 May 2003  
Entered Medline: 7 May 2003

AB We review the basic functions of neurotrophins and their receptors and discuss the expression and functions of neurotrophins and their specific receptors based on recent data using cultured cells from human periodontal tissues. Neurotrophins, nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and neurotrophin-3 (NT-3) play crucial roles in the differentiation and survival of neural cells. Neurotrophins activate 2 different receptor classes: the tropomyosin-related kinase (Trk) family of receptor tyrosine kinases (TrkA, TrkB, and TrkC) and the p75 receptor, a member of the tumor necrosis factor receptor superfamily. Neurotrophins regulate both cell death and cell survival through activations of Trk receptors and/or p75 neurotrophin receptor. It has been reported that neurotrophins are also produced from non-neuronal cells, such as leukocytes, osteoblasts, or fibroblasts, and act in many other ways on non-neuronal cells. Neurotrophin expression during bone fracture healing is especially interesting, and neurotrophins are now implicated in hard tissue regeneration. It is well known that neurotrophins and their receptors are expressed in tooth development. Recent studies have found that neurotrophins and Trk receptors are expressed in mouse osteoblastic cell lines. Human periodontal ligament cells, human gingival fibroblasts, and human gingival keratinocytes expressed mRNA for NGF and TrkA. The secretion of bioactive NGF peptides from human periodontal ligament cells and human gingival keratinocytes was confirmed by bioassay using PC12 cells (rat adrenal pheochromocytoma cells). The expression of NGF and TrkA mRNA was regulated by interleukin (IL)-1beta. NGF increased DNA synthesis and expressions of mRNA for bone-related proteins, alkaline phosphatase, and osteopontin in human periodontal ligament cells. Neurotrophins and Trk receptors expressed in human periodontal tissue may contribute to regeneration as well as innervation of periodontal tissue through local autocrine and paracrine pathways. Recent data suggest that some functions of neurotrophins and Trk receptors relate to periodontal disease and periodontal tissue regeneration. However, in vivo studies will be required to clarify the roles of neurotrophins and their receptors, including p75, in periodontal disease and periodontal tissue regeneration.

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L4 5 DUP REM L3 (11 DUPLICATES REMOVED)  
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L11 16 SEA FILE=MFE SPE=ON ABB=ON PLU=ON L10 AND NEUROTROPH?  
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L27	8 SEA FILE=MFE SPE=ON ABB=ON PLU=ON	L26 AND NEUROTROPH?	
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L29	3603 SEA FILE=MFE SPE=ON ABB=ON PLU=ON	SHINOHARA H?/AU	
L30	24 SEA FILE=MFE SPE=ON ABB=ON PLU=ON	L29 AND PERIODON?	
L31	5 SEA FILE=MFE SPE=ON ABB=ON PLU=ON	L30 AND NEUROTROPH?	
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DIS IBIB ABS L32 1-2

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COST IN U.S. DOLLARS			
FULL ESTIMATED COST		0.07	105.62
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)		SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE		0.00	-6.56

STN INTERNATIONAL LOGOFF AT 10:26:06 ON 10 JUN 2009